Cell Surface Immobilization of $GABA_A$Rs in Cerebellar Granule Cells Depends on the M3/M4 Cytoplasmatic Loop of the Alpha 1 Subunit

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Abstract

γ-Aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the vertebrate brain. The localization of GABA receptors type A ($GABA_A$Rs) at strategically located domains of the neuronal membrane is of vital importance for fast inhibitory synapse transmission efficacy. We have shown before that the lateral mobility of $GABA_A$Rs depends on subunit composition of the complex. To study the lateral mobility of $GABA_A$Rs in living, cultured neurons, we transfected cerebellar granule cells with either the complete α1 $GABA_A$R subunit or with a truncation of the α1 subunit that lacks the major intracellular loop (M3/M4). We examined the location and lateral mobility of receptors containing both versions of the α1 subunit in living neurons. From fluorescence recovery after photobleaching experiments we present novel evidences that the intracellular M3/M4 loop of the α1 subunit restricts the lateral mobility of $GABA_A$Rs when expressed in neurons. In addition, our immunocytochemical studies suggested that receptors containing the truncated subunit seem to be unable to reach synaptic localizations. Here we show for the first time that the α1 intracellular loop (M3/M4) domain has a relevant role in controlling the lateral mobility of $GABA_A$Rs in neurons, and we believe that this is a novel and important contribution in neurobiology of $GABA_A$ receptors.